

THE EFFECT OF PROPRANOLOL VERSUS PLACEBO ON RESIDENT SURGICAL PERFORMANCE*

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ABSTRACT

Purpose: To determine whether propranolol can decrease surgical tremor and anxiety in residents performing ocular microsurgery without impairing patient or physician safety.

Methods: In this randomized, double-masked, crossover study, 5 third-year ophthalmology residents ingested a capsule containing either propranolol, 40 mg, or placebo 1 hour prior to performing ophthalmic microsurgery. All residents were healthy men under age 30 years. Prior to commencement of the study, all participants had successfully been administered a test dose of propranolol without side effects. The study took place over a 10-week period. At the conclusion of each case, both the resident and attending surgeon observer independently completed a form grading, on a sliding scale: (1) amount of overall tremor; (2) amount of tremor during placement of the first 3 sutures after lens or nucleus extraction; (3) anticipated difficulty of the case; (4) actual difficulty with the case; and (5) anxiety (surgeon only). In addition, the type of procedure performed, complications encountered, and surgeon side effects were recorded. The data were analyzed with a 2-way analysis of variance for unbalanced data.

Results: A total of 73 surgical cases were performed; the surgeons were administered propranolol for 40 cases and placebo for 33. As judged by the resident surgeon, there was a highly significant effect of propranolol in decreasing anxiety ($P=.0058$), reducing surgical tremor overall ($P<.0001$), and reducing tremor while placing the first 3 sutures following lens extrac-

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tion ($P < .0001$). There was no treatment-by-surgeon interaction for any of the measures. Complications and difficulty of the case, as judged by both the resident and attending surgeons, were not significantly different in the propranolol versus placebo groups ($P > .05$). There were no side effects reported or observed in any of the surgeons.

Conclusions: Propranolol, 40 mg, administered 1 hour prior to surgery, significantly decreases tremor and anxiety in the surgeon without untoward effects to the surgeon and the patient. However, it is unknown whether decreased tremor and anxiety improve surgical outcome.

INTRODUCTION

Enhanced sympathetic activity is a typical response in the classic fight or flight situations.¹ However, excessive sympathetic stimulation may impair any delicate manipulation. Coordination may be adversely affected, and physiologic tremor and tachycardia from excessive catecholamine release may further exacerbate anxiety, establishing a spiraling cycle. Physiologic tremor increases in amplitude with anxiety and stress, probably through a sympathetic mechanism. It is well documented in normal subjects that sympathetic amines augment physiologic tremor through stimulation of beta-adrenergic receptors located in skeletal muscle.²⁻¹⁰ This enhancement of physiologic tremor can be completely blocked by low doses (10 to 40 mg) of propranolol.¹¹⁻¹³

Anxiety, which causes an outpouring of catecholamines, has been effectively treated with beta-adrenergic blocking drugs.^{14,15} These agents have been most useful in anxious patients with mainly somatic symptoms.^{16,17}

It is natural to extrapolate the use of beta-blocking agents to the potentially highly stressful situation of ophthalmologists performing microsurgery, for which skillful, complex, and delicate manipulations are necessary. A number of mechanical devices are commonly used to steady the hands and decrease the effect of surgical tremor.¹⁸ Recognizing the literature documenting a reduction in physiologic tremor and anxiety with beta-blocking agents and the potential of these agents in stressful situations, many ophthalmologists, as well as surgeons in other subspecialties, have begun taking these medications preoperatively to reduce tremor and anxiety in the hope of improving surgical performance. At our institution, an attending surgeon noted a decrease in surgical tremor after beginning propranolol therapy for the prophylactic treatment of migraine headaches. For these reasons, we thought it important to test the efficacy and safety of beta-blocking agents in reducing surgical tremor and intraoperative anxiety in residents performing ocular microsurgery.

METHODS

We performed a double-masked, crossover study designed to determine the effect of 40 mg of propranolol versus placebo on surgical tremor and intraoperative anxiety in residents performing ocular microsurgery. The selected dosage has been documented to reduce physiologic tremor induced by sympathetic amines without systemic side effects.¹³ The study was undertaken over a 10-week period during 1983. A schedule was drawn up that randomly assigned the resident to propranolol for 5 of the weeks and placebo for 5 of the weeks. When the study began, each resident had performed more than 60 intraocular microsurgical procedures.

Because any individual resident performs elective surgery at the University of Illinois only once a week, there was no problem with residual drug effect. A departmental and institutional review board at the University of Illinois approved the protocol for the study. Prior to entry into the study, each resident was administered an oral test dose of 40 mg of propranolol and responded without adverse reaction. A history of bronchial asthma excluded one resident from participation. All participants were healthy men less than 30 years old; none required any long-term medication.

During the 24 hours before surgery, the resident surgeon refrained from ingesting caffeine, alcohol, or medication. On the day of surgery, he ingested a capsule containing either 40 mg of propranolol or placebo approximately 60 minutes before his first operative case. At the conclusion of each case, both the resident and attending surgeon observer independently completed a form by grading on a sliding scale: (1) amount of overall tremor, (2) amount of tremor during placement of the first 3 sutures after delivery of the lens or lens nucleus (in accordance with the prevailing surgical technique at the time the study was performed), (3) anticipated difficulty of case, (4) actual difficulty of case, and (5) anxiety (surgeon only). In addition, the procedure performed, complications encountered, and other data were recorded.

The data were analyzed with a 2-way analysis of variance for unbalanced data.¹⁹

RESULTS

Three residents completed the entire study. Two other residents participated for less than the full 10-week period. A total of 73 cases were performed (Table I); the surgeons took propranolol for 40 cases and placebo for 33. The results showing resident and attending surgeon ratings are presented in Figs 1 and 2. There was no treatment-by-surgeon interaction for any of the measures. As judged by the resident surgeon, there was a

TABLE I: CASES PERFORMED

PROCEDURE	PROPRANOLOL	PLACEBO
Extracapsular cataract extraction	14	10
Extracapsular cataract extraction with implantation of intraocular lens	12	14
Intracapsular cataract extraction	2	1
Phacoemulsification	1	0
Cataract extraction with vitrectomy	2	3
Trabeculectomy	2	2
Vitrectomy	2	1
Iridectomy	2	1
Retinal detachment surgery	2	1
Scleral laceration repair	1	0
Total	40	33

highly significant effect of propranolol in decreasing anxiety and in reducing overall surgical tremor and tremor when corneal-scleral sutures were first placed for cataract surgery. When the data from the 2 surgeons who did not complete the study were deleted from the analysis because of the relatively few operations performed, the treatment effect still held to the same level of statistical significance (Table II). Difficulty of the case, as judged by the resident and attending surgeons, was not significantly different in the propranolol versus placebo group ($P > .05$).

When the data from all attending surgeons' gradings of tremor were pooled, they did not show a statistically significant difference between the propranolol and placebo groups for any variable. However, in grading overall tremor, a possible treatment effect was suggested. There were several factors that made the attending data difficult to analyze. First, the cases were randomized with respect to the resident surgeon but not to the attending surgeon. Second, a total of 11 attending surgeons observed different residents; of these, only 3 observed more than 10 cases. One

TABLE II: TREATMENT EFFECT OF PROPRANOLOL VERSUS PLACEBO IN THREE RESIDENT SURGEONS

VARIABLE	RESIDENT	ATTENDING
Tremor overall	$P < .0001$	$P = .0824$
Tremor first three sutures	$P < .0001$	$P = .132$
Anxiety	$P = .0058$	—
Anticipated difficulty	$P = .67$	$P = .22$
Actual difficulty	$P = .33$	$P = .109$

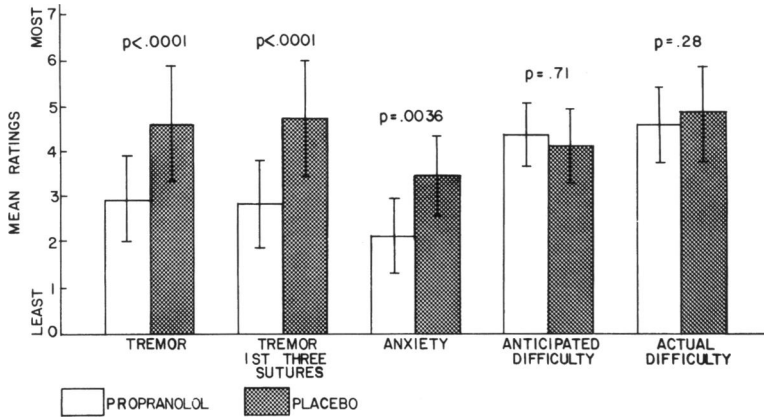


FIGURE 1

Mean scores as judged by resident surgeons.

attending surgeon observed 7 cases, for which all the residents had received propranolol. Only 1 attending surgeon observed 1 resident for more than 15 cases. Among his observations, significantly less tremor was observed in the propranolol versus placebo group ($P = .033$).

DISCUSSION

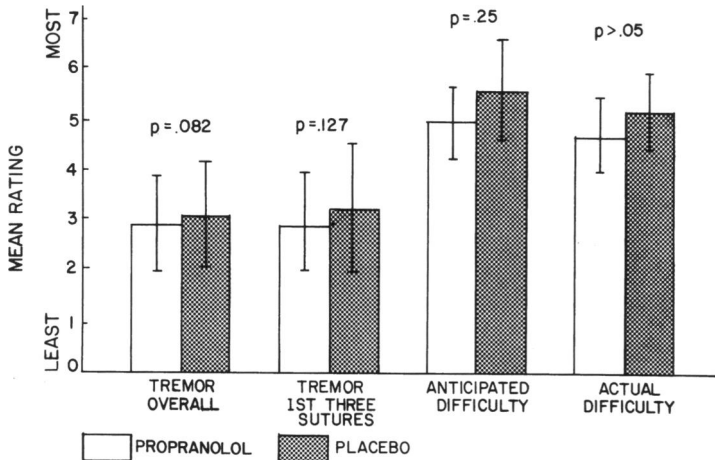


FIGURE 2

Mean scores as judged by attending surgeons.

DISCUSSION

Tremor is defined as an involuntary oscillatory movement produced by alternating contraction of muscle groups and their reciprocally innervated antagonists.²⁰ Physiologic tremor, present in all normal persons, involves the limbs, head, and tongue.²¹ It is of low amplitude, is usually asymptomatic, and has a frequency that varies from 6 to 12 Hz in adults. It is best observed in the outstretched fingers when the wrists are hyperextended and the arms are held away from the body.²² Electromyography shows poor synchronous activity. Anxiety, stress, and sympathomimetic drugs increase the amplitude of physiologic tremor, presumably by synchronizing the motor unit discharges.²⁰ Peripheral beta-adrenergic receptors seem to play a key role in mediating the amplitude of physiologic tremor.⁶⁻⁹ Beta-blocking agents decrease the amplitude of physiologic tremor.¹⁰⁻¹³

Physiologic tremor largely affects surgical instrument stability, presumed to be so crucial to success in microsurgery. Humayin and associates²³ showed that low doses of propranolol can decrease physiologic surgeon hand tremor in a laboratory setting. This is the first study that demonstrates that propranolol can significantly diminish physiologic surgeon hand tremor in ophthalmologists under actual surgical conditions.

The mechanism by which beta-blocking drugs act in the treatment of anxiety is still not fully resolved. As with physiologic tremor, the chief mechanism appears to be peripheral beta blockade. However, the evidence for this is more circumstantial.²⁴⁻²⁹ The main clinical effects of beta blockers in reducing anxiety appear to be in decreasing somatic and autonomic symptoms, which are believed to be mediated by peripheral beta receptors.^{2,16} A double-masked crossover trial in 24 musicians showed the efficacy of a beta-blocking agent in significantly improving musical performance, particularly at the first performance, and in those most affected by anxiety.³⁰

Unlike alcohol and benzodiazepine drugs, propranolol significantly decreases anxiety and tremor without impairing higher central nervous system functions.²⁹ For this reason, alcohol and benzodiazepine drugs would be impractical and, indeed, unethical in a surgical setting. Propranolol has the added advantage of not producing dependence in any form.

In our study, 40 mg of propranolol significantly decreased surgical tremor and anxiety, at least as rated by the resident surgeon. The difficulty of the cases did not differ significantly between the propranolol and placebo groups. The difference in tremor scores in the placebo and propranolol groups was less striking when viewed by all the attending surgeons. The study design makes the attending gradings difficult to interpret. It would have been desirable to have the same attending surgeons

observe all cases with the same resident. Unfortunately, this was not possible in designing the protocol. It is possible that the decrease in tremor may be primarily a perceived effect on the part of the surgeon. Another possible explanation is that an actual effect occurred, but the attending surgeons were inadequate observers. As judged from the evaluation by the single attending surgeon observing the same resident each week, propranolol decreased surgical tremor markedly in that resident. The attending surgeon grading notwithstanding, the highly significant treatment effect of propranolol in decreasing surgical tremor and anxiety as viewed by the surgeon was most striking.

While many surgeons have noticeable tremor but nevertheless achieve good surgical results, certainly some surgeons may benefit from preoperative propranolol. One such group may be senior ophthalmic surgeons who are contemplating curtailing surgery because of increasing tremor with age. Of course, caution must be exercised in extrapolating our data to this or any group; our results were in small group of healthy men under age 30. The efficacy and safety of preoperative propranolol in more senior surgeons have not been examined. Many may already be taking beta blockers for cardiac indications and may be the unwitting beneficiaries of decreased tremor. Although no untoward effects were reported by any of the resident surgeons, a thorough medical and cardiovascular evaluation with and without propranolol would be wise before this medication is used in the operating room, particularly in older surgeons. We must emphasize that in the unlikely event that a serious reaction from propranolol would have occurred in the operating room, our resident surgeons had experienced backup surgeons in the attending observers. Similar precautions would be necessary for any surgeon beginning to use propranolol during surgery.

Although reducing physiologic hand tremor empirically improves surgical instrument stability, the important question that must be answered is whether decreasing anxiety or surgical tremor actually affects surgical outcome. Although this was beyond the scope of our study, several points can be made in this regard. There was no significant difference in the complications reported in the propranolol versus placebo group. Certainly, many factors in addition to surgical tremor may lead to serious complications, such as vitreous loss. Indeed, 2 such cases involved a subluxated lens, a known risk factor for vitreous loss. Given the low frequency of surgical complications even in resident cases, our study lacked sufficient sample size and statistical power to detect a small difference in complication rate, if it exists.

While final visual acuities and postoperative complications were not evaluated, it was the impression of the participating surgeons that all patients did equally well. In fact, after the results of the study became known, all participating surgeons thought that the possible improvement

in surgical performance did not warrant routine preoperative propranolol use because the patients' intraoperative complication rate and final visual results appeared to be the same. Furthermore, the residents had learned to adapt their surgical technique to minimize the effects of any pronounced tremor.

Ingestion of a low dose of propranolol 1 hour before surgery decreases surgeon hand tremor and anxiety without noticeable side effects. Caution must be exercised in extrapolating these results in a small group of young, healthy men to others. Finally, we presume that decreasing tremor and anxiety should improve surgical performance. However, the effect of decreasing surgical tremor and anxiety, by any means, on surgical outcome and final visual acuity remains untested and unknown.

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DISCUSSION

DR JULIA A. HALLER. Dr Elman and coauthors have presented an extremely interesting, well-designed trial of the use of a single preoperative dose of propranolol to reduce resident tremor and anxiety during cataract surgery. Residents completed a 10-week course during which they ingested either 40 mg of propranolol or a placebo pill prior to surgery and then evaluated their own levels of anxiety, tremor, and perceived difficulty of the case. Attending surgeons' evaluations of resident tremor and case difficulty were also recorded.

This study has a number of advantages, many of them due to good initial protocol design. It was conducted prospectively, in randomized, double-masked fashion, with a placebo control. It produced statistically significant positive results in at least one area: the resident surgeons noted a decrease in anxiety and tremor when dosed with propranolol before cataract surgery.

Some of the study's disadvantages are that it involved a small number

of residents — only 3 completed the entire protocol, although we have the benefit of data on an additional 2 who participated for less than the full 10-week period — and that there was no objective measurement of the end points. We know that the residents perceived that their tremors decreased with propranolol, but we do not know whether the tremor actually did change or whether the perception was a result of less anxiety or a lower pulse rate or some other factor. The “objectivity” in the study was intended to be the observations of the attending physicians staffing the resident cases, but unfortunately this evaluation was not uniformly completed owing to the understandable inability to schedule attending surgeons predictably to observe the same resident under both placebo and beta blocked conditions.

Humayun and associates¹ have also studied the effect of beta blockade on surgical tremor in ophthalmologists, quantifying the change in tremor in a simulated surgical situation by use of the Microsurgical Advanced Design Laboratory's Stability, Activation, and Maneuverability tester (MADSAM). These investigators also found that propranolol significantly decreased tremor when objectively measured in the laboratory.

Numerous factors have an impact on microsurgical technique, among which hand tremor may be significant. Certainly, a perception that tremor is deleterious underlies our efforts to minimize tremor during eye surgery with stabilizing devices such as wrist and hand rests. Similarly, many surgeons avoid coffee on the morning of surgery.

Tremor increases with stress and anxiety, as well as following physical exertion and fatigue. Amplitude of tremor also increases in the settings of increased norepinephrine release, nicotine ingestion, and caffeine intake. Beta blockade with agents such as propranolol effectively reduces essential tremor.^{2,3}

Eye surgeons are not the only group seeking to improve results by reducing tremor. Studies have also evaluated the benefit of a beta blocker in other professionals, including actors, musicians, athletes, and precision pistol marksmen. The effects of drug administration before performance are those expected with blockade of the beta receptor. The pharmacologic response includes anxiety reduction and decrease in heart rate, blood pressure, and tremor.¹ What is less clear is whether or not this physiologic change translates into more dramatic soliloquies, more soaring violin concertos, more bull's-eye shots, or better visual outcomes with cataract surgery.

Is there any danger in taking beta blockers? In this study, asthmatics were excluded and all participants were young and healthy. This group of surgeons may very well be able to take beta blockers sporadically without undue ill effect. The authors are commendably cautious in extrapolating their data to other groups but suggest that the drug may be useful for

senior ophthalmic surgeons who have increasing tremor with age. Consultation with my colleagues in cardiology suggests, however, that continual up-and-down regulation of the beta receptor may well be unwise, particularly in older individuals with a higher likelihood of underlying cardiac and/or ischemic disease.

Certainly, there are nonpharmacologic strategies available to optimize cataract surgery, some of which also decrease tremor. In the case of younger surgeons, practice with animal and eye-bank eyes, careful preoperative preparation, and the reassurance of an experienced and capable assistant may be safer and possibly, over the long run, better means of decreasing anxiety and tremor, compared with beta blockade.

As a resident, I had the opportunity to perform some of my first cases with the late Dr A. Edward Maumenee. He was well known for his approach to the nervous tremor of the inexperienced resident surgeon. If the resident had very little tremor, "The Prof" would exclaim, "Amazing! No tremor at all!" But if the resident had a terrible tremor, he was equally reassuring and encouraging. "Anyone who cares about his patient," he would say, "has a tremor." Needless to say, in either case the resident immediately felt more confident, and his or her heart rate and blood pressure — and tremor amplitude — decreased.

This paper by Dr Elman and coauthors persuasively expands the data base showing that propranolol given before a performance of any kind does indeed produce the expected effects from blockade of the beta receptor. It inspires further trials to demonstrate improved outcomes and long-term safety and to elucidate optimum candidates for treatment. I would like to ask Dr Elman if he routinely recommends propranolol currently, and, if so, to whom. Certainly, we all see the occasional resident or fellow who might benefit from beta blockade in the early phases of a surgical career. For the most part, however, I would suggest that other nonpharmacologic methods, such as those practiced by outstanding mentors like Dr Maumenee, may offer a safer and more reliable long-term approach to the problem of surgical anxiety and tremor.

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MALCOLM LUXENBERG, MD. I want to thank Dr Elman for his paper. I would like to ask him if they considered using sublingual beta blockers

such as one or two drops of Timolol, which can achieve the same results and also be used in emergency situations for certain cardiac arrhythmias.

ROBERT DREWS, MD. Another problem, if one is doing a lot of surgery on the same day, is having gloves that are too tight. Sometimes changing to a larger glove can reduce one's tremor.

MICHAEL ELMAN, MD. I wish to thank Dr Haller for her remarks. I agree with her about the importance of mentorship. I would like to share an anecdote with you. Certain attending surgeons in my residency program were known to be stress provoking. The degree of tremor was higher in both the treated and the placebo groups when working with these attending surgeons. One attending surgeon provoked so much stress that we routinely put our patients to sleep whenever he was the attending physician. I've had the great fortune of working with a number of outstanding mentors. The most important thing the attending surgeon needs to do is to instill confidence in the trainee. In this study, we had the advantage of having an excellent attending surgeon for backup in case the beta blocker produced any problems. In outside situations, we do not have this luxury. With respect to Dr Luxenburg's comment, we did try sublingual Timolol. In fact, our chief resident had tried this in the past. We did not use it in this study because it would have unmasked the study. I therefore cannot comment on the efficacy of Timolol but it apparently tastes awful. I appreciate Dr Drews' comment about tight surgical gloves and agree that this could occasionally be a problem.